REMARKS

Claims 28-38, 41, 55 and 56 are pending. Claim 28 is amended to clarify that the proanthocyanidin constitutes at least 70 % of an active component of the composition and claim 55 is amended to clarify that the mixture of proanthocyanidins constitutes at least 70 % of an active component of the composition.. The amendment finds basis in the specification as originally filed. For example, the specification states on page 11, line 19 through page 12, line 17, that the proportion percentage or percent purity of proanthocyanidins in the claimed compositions significantly exceeds the proportion percentage of proanthocyanidins in natural presence in a plant or a plant extract. The specification further states on page 40, lines 24-28 that the proanthocyanidins in the claimed compositions is at least 70% pure proanthocyanidin.

No new matter is added.

THE REJECTION OF CLAIMS 28-41 and 55-56 UNDER 35 U.S.C. §102(b), OVER KUZNICKI *ET AL.*

Claims 28-41 and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kuznicki *et al.* (U.S. Patent No. 5,681,569) because the cited reference allegedly discloses a composition containing green tea solids extracted from tea material. The extract contains 0.01-0.35% flavanols and catechins, wherein the catechin or a mixture of two or more catechins are catechin, epicatechin, gallocatechin, epigallocatechin gallate and epicatechin gallate, and a pharmaceutical carrier. The Office Action alleges that the green tea composition of Kuznicki *et al.* inherently contains proanthocyanidin oligomers having the instant formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

The Office Action alleges that the inherency of the green tea composition is supported by the Hashimoto *et al.* The Office Action urges that Hashimoto *et al.* discloses that proanthocyanidins are isolated from oolong tea. It is alleged that oolong tea is a well known green tea. The Office Action alleges that the compounds identified by Hashimoto *et al.* in the green tea compositions are the instant compounds having formula I or II.

The Office Action further alleges that Morimoto *et al.* also teaches proanthocyanidin containing compositions wherein the proanthocyanidins can be degraded to catechins and epicatechins.

Applicants note that claims 39 and 40 were cancelled in the previous response (Filed August 23, 2005). The rejection is respectfully traversed with respect to pending claims 28, 31-38, 41 and 55-56.

Disclosure of Kuznicki *et al.*

Kuznicki *et al.* discloses a liquid composition containing flavanols from green tea extract, sodium and potassium ions, carbohydrate and water. The reference also discloses a dry composition containing flavanols from green tea extract, sodium and potassium ions, carbohydrate (column 2, lines 12-32). The reference further discloses that the term flavanol or catechin means primarily catechin, epicatechins, and their derivatives (column 3, lines 20-21). The reference discloses that the derivatives include sugar, salts, sugar esters, and other edible physiologically available derivatives. It is further described in the reference that the flavanols used therein can be extracted from fruits, vegetables, green tea or other natural sources (column 4, lines 9-11). The reference discloses that the drinkable beverage contains about 0.01% to 0.035% unoxidized, unpolymerized flavanols.

Differences between the claimed subject matter and the disclosure of Kuznicki *et al.*

Claims 28-38 and 41

Applicants note that amended claim 28 is directed to a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition,

Applicants have previously argued there is no record that indicates the presence of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II in green tea. Applicants further provided several references (with the response dated October 14, 2004) that record various components of green tea. Furthermore, the cited reference by Kuznicki *et al.* discloses that the components of green tea are catechin, epicatechin,

gallocatechin, epigallocatechin, epicatechin gallate, epigallocatechin gallate. The reference also discloses that the drinkable beverage disclosed therein contains 0.01% to about 0.03% **unoxidized, unpolymerized flavanols**. The reference does not disclose that the proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II is present in the green tea extract.

The Office Action does not provide any evidence that the proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II is present in the green tea extract. However, even assuming *arguendo*, that the green tea contains proanthocyanidins of the instant composition, there is no disclosure in the reference that the proanthocyanidin constitutes at least 70% of an active component in the drinkable beverage disclosed therein. As discussed above, the reference discloses that the drinkable beverage disclosed therein contains 0.01% to about 0.03% unoxidized, unpolymerized flavanols. It further discloses that beverage contains caffeine. Kuznicki *et al.* does not disclose that the proanthocyanidin constitutes at least 70% of an active component in the drinkable beverage as claimed instantly.

Applicants respectfully submit that the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). In the instant case, the cited reference by Kuznicki *et al.* discloses compositions containing green tea extract. Neither Kuznicki *et al.* nor any other reference of record discloses that the proanthocyanidin constitutes at least 70% of an active component in green tea as instantly claimed.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Kuznicki *et al.* does not anticipate a composition wherein the proanthocyanidin constitutes at least 70% of an active component in the composition as claimed in claim 28. Because claims 29-38 and 41 depend from claim 28, Kuznicki *et al.* does

not anticipate any of the claims dependent on claim 28. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Claim 55 is directed to a pharmaceutical composition containing therapeutically effective amount of a mixture selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins wherein the mixture constitutes at least 70% of an active component of the composition.

Applicants respectfully submit that the cited reference does not disclose, either literally or inherently, a pharmaceutical composition containing therapeutically effective amount of a mixture of proanthocyanidins selected as described in claim 55. Further, the reference does not disclose a pharmaceutical composition containing therapeutically effective amount of a mixture of proanthocyanidins selected as described above wherein the mixture constitutes at least 70% of an active component of the composition.

The Office Action alleges that the disclosed compositions contain catechins extracted from green tea and their percentage purity is known to significantly exceed a proportion percentage of the catechin present in a plant. As discussed above, the compositions containing the green extract disclosed in the reference do not contain a mixture of proanthocyanidins, wherein the mixture constitutes at least 70% of an active component of the composition as described in the instant claims.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Kuznicki *et al.* does not anticipate claim 55. Because claim 56 depends from claim 55, Kuznicki *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Disclosure of Hashimoto *et al.* and Morimoto *et al.*

The Office Action appears to support the allegation of inherency based on the teachings Hashimoto *et al.* and Morimoto *et al.* The Office Action alleges that the oolong tea composition in Hashimoto *et al.* inherently comprises the instant compounds because these compounds are known to be isolated from oolong tea. It is further alleged that Morimoto *et al.* teaches

proanthocyanidins or procyanidins wherein proanthocyanidins can be degraded to catechins and epicatechins.

Hashimoto *et al.* discloses components of oolong tea extract in 80% aqueous acetone. The reference describes that the 80% aqueous acetone extract of oolong tea contains flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. Morimoto *et al.* discloses components of *Illicium anisatum* extract in 80% aqueous acetone. The reference discloses that the 80% aqueous acetone extract of *Illicium anisatum* contains several procyanidins, including compounds of formula I and II. The reference does not disclose components of green tea extract.

Applicants respectfully submit that the instant claims are directed to pharmaceutical compositions containing a proanthocyanidin or a mixture of proanthocyanidins selected as described in the instant claims. The claims are not directed to proanthocyanidins or procyanidins. Therefore, as further discussed below, the fact that Hashimoto *et al.* describes **80% aqueous acetone extract** of oolong tea contains flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins or Morimoto *et al.* describes the presence of several procyanidins, including compounds of formula I and II in **80% aqueous acetone extract** of *Illicium anisatum* is not relevant to the instantly claimed compositions.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. §102(b) OVER JP 10245342

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by JP 10245342 because the reference allegedly discloses a pharmaceutical composition for diminishing the toxicity in nerve cells caused by β-amyloid protein containing a catechin or two or more of catechin such as epigallocatechin gallate and epicatechin gallate prescribed in effective amounts for diminishing the toxicity of β-amyloid protein, and a pharmaceutical carrier. The Office Action alleges that the green tea composition disclosed in the cited reference inherently contains proanthocyanidins oligomers having formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

The rejection is respectfully traversed with respect to pending claims 28, 31-38, 41 and 55-56.

Disclosure of JP 10245342

JP 10245342 discloses that green tea extract contains polyphenols such as tea catechin and/or theaflavin. The reference describes that the composition containing tea catechins and/or theaflavin can be used for diminishing the toxicity in nerve cells caused by β-amyloid protein. The reference does not disclose, inherently or literally, a composition wherein proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts thereof constitute at least 70% of an active component of the composition as claimed in claim 28.

Differences between the claimed subject matter and the disclosure of JP 10245342

Claims 28 and 31-41

The compositions disclosed in JP 10245342 do not contain proanthocyanidins selected as described in the instant claims. The reference clearly describes that the compositions contain tea catechin and/or theaflavin extracted from green tea. As discussed above, there are no references of record to indicate that green tea extract contains a proanthocyanidin selected from the compounds of formula I or II or the oligomeric combinations thereof. Further, there is no disclosure in the reference that the proanthocyanidin constitutes at least 70% of an active component in the green tea composition disclosed therein.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, JP 10245342 does not anticipate the composition claimed in claim 28. Because claims 31-38 and 41 depend from claim 28, JP 10245342 does not anticipate any of the claims dependent on claim 28. Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claim 55-56

Further, the reference does not disclose a pharmaceutical composition containing a mixture of proanthocyanidins, where the proanthocyanidin is selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts thereof and wherein the mixture constitutes at least 70% of an active component of the composition.

Applicants respectfully submit that the cited reference does not disclose, either literally or inherently, a pharmaceutical composition containing therapeutically effective amount of a mixture of proanthocyanidins selected as described above wherein the mixture constitutes at least 70% of an active component of the composition. Therefore, the reference does not anticipate the composition claimed in claim 55. Because claim 56 depends from claim 55, the reference does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. § 102(b) OVER HASHIMOTO *ET AL.*

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hashimoto *et al.* because Hashimoto *et al.* allegedly discloses a composition containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers or proanthocyanidins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the oolong tea composition in Hashimoto *et al.* inherently comprises the instant compounds because these compounds are known to be isolated from oolong tea. The rejection is respectfully traversed.

Disclosure of Hashimoto *et al.*

Hashimoto *et al.* discloses that polyphenolic constituents in the **80% aqueous acetone extract** of oolong tea include flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. The reference does not disclose a pharmaceutical composition that contains a therapeutically effective amount of proanthocyanidins as instantly claimed.

Differences between the claimed subject matter and the disclosure of Hashimoto *et al.*

Claim 28 and 31-38 and 41

Hashimoto *et al.* describes an oolong tea extract in 80% aqueous acetone containing polyphenolic constituents including proanthocyanidins. It does not describe a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically

acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition, and the therapeutic amount of the proanthocyanidin is selected for efficacy in treating amyloid, α -synuclein or NAC fibrillogenesis in a mammalian subject.

The instantly claimed pharmaceutical compositions contain a therapeutically effective amount of a proanthocyanidin, and a pharmaceutically acceptable carrier. The reference does not disclose a pharmaceutically acceptable carrier, diluent, or excipient, as required in the instantly claimed compositions. As well known in the art, 80% aqueous acetone disclosed in the reference is not a pharmaceutically acceptable carrier. Therefore, oolong tea extract in 80% aqueous acetone containing proanthocyanidins is not within the scope of the instantly claimed pharmaceutical composition.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Hashimoto *et al.* does not anticipate the pharmaceutical composition as claimed in claim 28. Because claims 31-38 and 41 depend from claim 28, Hashimoto *et al.* does not anticipate claims 31-38 and 41. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Hashimoto *et al.* further does not disclose a pharmaceutical composition containing a mixture of proanthocyanidin, where the proanthocyanidin is selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts thereof and wherein the mixture constitutes at least 70% of an active component of the composition as claimed in claim 55. As discussed above, the reference describes oolong tea extract containing proanthocyanidins in 80% aqueous acetone.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Hashimoto *et al.* does not anticipate the composition claimed in claim 55. Because claim 56 depends from claim 55, Hashimoto *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Rebuttal to Examiner's Arguments

The Office Action alleges that Hashimoto *et al.* discloses catechins extracted and isolated from teas or other plants. It is urged that the percentage purity therein is known to significantly exceed a proportion percentage of the catechin present in a plant.

Applicants respectfully submit that Hashimoto *et al.* describes that components of oolong tea extract in 80% aqueous acetone were isolated. The reference further discloses polyphenolic constituents in the 80% aqueous acetone extract of oolong tea include flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. The reference does not disclose a pharmaceutical composition containing a mixture of proanthocyanidins and a **pharmaceutically acceptable carrier** as instantly claimed.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. §102(b), OVER MORIMOTO *ET AL.*

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Morimoto *et al.* because Morimoto *et al.* allegedly discloses a composition containing a catechin or two or more catechins such as epigallocatechin and dimers and procyanidins in effective amounts and in pharmaceutical carrier. The Office Action urges that the compounds identified by Morimoto *et al.* are allegedly the instant compounds of formula I and II. The rejection is respectfully traversed.

Disclosure of Morimoto *et al.*

Morimoto *et al.* discloses components of *Illicium anisatum* extract in 80% aqueous acetone. The reference discloses that the 80% aqueous acetone extract of *Illicium anisatum* contains several procyanidins, including compounds of formula I and II. The reference does not disclose a pharmaceutical composition containing a pharmaceutically acceptable carrier.

Differences between the claimed subject matter and the disclosure of Morimoto *et al.*

Claim 28 and 31-38 and 41

Morimoto *et al.* describes that *Illicium anisatum* extract in **80% aqueous acetone** contains several procyanidins, including compounds of formula I and II. It does not describe, inherently or literally, a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by

Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition, and the therapeutic amount of the proanthocyanidin is selected for efficacy in treating amyloid, α - synuclein or NAC fibrillogenesis in a mammalian subject. Applicants respectfully submit that 80% aqueous acetone is not a pharmaceutically acceptable carrier. Therefore, the *Illicium anisatum* extract in 80% aqueous acetone containing procyanidins is not within the scope of the instantly claimed pharmaceutical composition.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Morimoto *et al.* does not anticipate the composition claimed in claim 28. Because claims 31-38 and 41 depend from claim 28, Morimoto *et al.* does not anticipate claims 31-38 and 41. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Morimoto *et al.* further does not disclose a pharmaceutical composition containing a mixture of proanthocyanidins, where the proanthocyanidin is selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts thereof and wherein the mixture constitutes at least 70% of an active component of the composition. As discussed above, the reference describes extract of *Illicium anisatum* containing procyanidins in 80% aqueous acetone.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Morimoto *et al.* does not anticipate the composition claimed in claim 55. Because claim 56 depends from claim 55, Morimoto *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

In response to the allegation in the Office Action that the compounds identified by Morimoto *et al.* are the instant compounds of formula I and II, applicants respectfully submit that

the instant claims are directed to a pharmaceutical composition containing the proanthocyanidins as described in the instant claims and a pharmaceutically acceptable carrier. The claims are not directed to compounds of formula I and II. Therefore, presence of the compounds of formula I and II in 80% aqueous acetone extract of *Illicium anisatum* does not anticipate the instantly claimed compositions.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. §102(b), OVER HATANO *ET AL.*

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hatano *et al.* because Hatano *et al.* allegedly discloses a composition for anti-HIV containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers of proanthocyanidins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the compositions in the cited reference inherently contains the instant compounds because these compounds are known to be isolated from Camellia japonica plants. The rejection is respectfully traversed.

Disclosure of Hatano *et al.*

Hatano *et al.* discloses eight tannins isolated from the leaf of Camellia japonica. The reference further discloses that the tannins isolated include complex tannins consisting of monomeric hydrolysable tannin and epicatechin, dimeric hydrolysable tannins and complex tannins composed of a dimeric hydrolysable tannin and epicatechin. The reference further discloses that the tannins isolated showed anti-HIV activity.

Differences between the claims and the disclosure of Hatano *et al.*

Claims 28, 31-38 and 41

Hatano *et al.* does not describe, inherently or literally, a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, wherein proanthocyanidin constitutes at least 70% of an active component of the composition and the therapeutic amount of the proanthocyanidin is selected for efficacy in

treating amyloid, α -synuclein or NAC fibrillogenesis in a mammalian subject as described in claim 28. Hatano *et al.* discloses that an extract from leaf of Camellia japonica contains complex tannins consisting of monomeric hydrolysable tannin and epicatechin, dimeric hydrolysable tannins and complex tannins composed of a dimeric hydrolysable tannin and epicatechin. The reference does not disclose, inherently or literally, that the proanthocyanidin constitutes at least 70% of an active component of the leaf extract.

Thus, the cited reference does not disclose every element of the claimed composition. Therefore, Hatano *et al.* does not anticipate the composition claimed in claim 28. Because claims 31-38 and 41 depend from claim 28, Hatano *et al.* does not anticipate claims 31-38 and 41. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Hatano *et al.* further does not disclose a pharmaceutical composition containing a mixture of proanthocyanidins, where the proanthocyanidin is selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts thereof, wherein the mixture constitutes at least 70% of an active component of the composition as claimed in claims 55 and 56. As discussed above, the reference discloses an extract from Camellia japonica containing tannins. The reference does not disclose that the active component in the extract contains a mixture of at least 70% proanthocyanidins as described in the instant claim.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Hatano *et al.* does not anticipate the composition claimed in claim 55. Because claim 56 depends from claim 55, Hatano *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

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In view of the amendments and remarks herein, reconsideration and allowance of the application are respectfully requested.

Applicant hereby petitions under 37 C.F.R. §1.136 for two (2) months extension of time. Please apply fees for the extension of time and Notice of Appeal ($225.00 + $250.00 = $475.00) and any other charges, or any credits, to Deposit Account 50-3013.

Respectfully submitted,

Date: 3/22/06

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